ORIGINAL ARTICLE

TNF antagonists in the treatment of inflammatory bowel disease: Results of a survey of gastroenterologists in the French region of Lorraine

Les anti-TNF dans le traitement des maladies inflammatoires chroniques intestinales : résultats d’une enquête de pratique en Lorraine

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Summary

Background and objective. — We conducted a survey of nonacademic gastroenterologists to evaluate the use of tumor necrosis factor (TNF) antagonists in inflammatory bowel disease (IBD).

Methods. — A total of 100 questionnaires were sent by mail to a representative sample of gastroenterologists practicing in the French region of Lorraine.

Results. — Forty-six practitioners responded to the survey, of whom 95.5% prescribed scheduled infliximab treatment. After 6 months of infliximab in combination with azathioprine, 55% then prescribed infliximab as monotherapy. A complete pretherapeutic assessment was performed by only one fourth of the gastroenterologists. When the PPD skin test measured 7 mm, nearly half of the physicians introduced anti-TNF therapy without chemoprophylaxis (versus only 2.4% when the diameter was 11 mm). In the event of quiescent Crohn’s disease (CD) after 1 year of anti-TNF treatment, 35.7% stopped the drug. In refractory CD, 72.7% prescribed infliximab as the first-line therapy (versus 27.3% who used adalimumab). In patients with urinary tract infection, 44.2% initiated antibiotics and delayed anti-TNF treatment, while 46.5% initiated anti-TNF therapy along with antibiotic therapy.

Conclusion. — This study is the first survey upon the use of TNF antagonists by nonacademic gastroenterologists, and the findings suggest that physicians using these drugs may require more information about the pretherapeutic assessment and management of the infectious risk.

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Introduction

In the mid-1990s, the advent of biotherapy drugs—in particular, tumor necrosis factor antagonists (anti-TNF)—revolutionized the treatment for drug-resistant inflammatory bowel disease (IBD). Anti-TNF drugs have clearly demonstrated their efficacy in this patient population, reducing the need for surgery and the number of hospital admissions, allowing steroid withdrawal, improving patients’ quality of life and even, in certain patients, enabling endoscopic healing of the inflammatory mucosa [1]. At present in Europe, only infliximab and adalimumab have marketing approval for IBD. Anti-TNF drugs have clearly demonstrated their efficacy in this patient population, reducing the need for surgery and the number of hospital admissions, allowing steroid withdrawal, improving patients’ quality of life and even, in certain patients, enabling endoscopic healing of the inflammatory mucosa [1]. At present in Europe, only infliximab and adalimumab have marketing approval for IBD, although certolizumab pegol is also available for Crohn’s disease (CD) in the United States [2,3]. In France, infliximab was the first anti-TNF to obtain marketing approval for CD resistant to conventional drugs (mainly corticosteroids and immunosuppressors) [2]. In 2005, infliximab was also approved for luminal and fistulizing CD as well as for ulcerative colitis (UC), whereas adalimumab is indicated solely for refractory luminal CD [2].

While certain practices regarding the use of biotherapy for IBD are based on solid scientific evidence—for example, the use of infliximab for complex anoperineal fistulae [4,5], and the need to maintain treatment by intravenous infusions (infliximab) or subcutaneous injections (adalimumab) in initial responders [6,7]—other practices are largely or exclusively based on expert opinion only. This means that a number of questions remain open:

- when should anti-TNF treatment be discontinued?
- should long-term immunosuppressive treatment be associated with infliximab?
- which is the most appropriate anti-TNF for first-line treatment of refractory luminal CD?

Given this situation, we believed it would be useful to learn more about the actual practices of nonacademic gastroenterologists to obtain an up-to-date picture of the use of anti-TNF in IBD. To our knowledge, there are no data in the literature on this topic. The results of our survey highlight the requirement for better information for practitioners who prescribe anti-TNF for IBD and the need to focus attention on the importance of developing uniform treatment practices.

Material and methods

Study design

This mailed-out survey, using a questionnaire developed by the Nancy University Hospital Department of Hepatogastroenterology, was posted to all nonacademic gastroenterologists in the Lorraine region of France. The study was coordinated by the Department, which furnished the practitioners’ addresses and a covering letter, detailing the objectives of the survey, included with the confidential questionnaire. The practitioners could return the completed questionnaire by mail or by fax to the Department’s secretarial service. The questionnaire was posted first in January 2008 and again in April 2008 to physicians who had not yet responded.

The questionnaire

Based on an exhaustive review of the literature on the topic, a specially designed questionnaire on the use of anti-TNF in the treatment of IBD, called Enquête Anti-TNF et MICI (Anti-TNF and IBD survey), was devised by two academic gastroenterologists (L. P.-B. and M.-A. B.) who regularly prescribe anti-TNF at the Nancy University Hospital (more than 500 patients with IBD treated by anti-TNF since January 2008; personal data).

The questionnaire was divided into three parts. The first part obtained information about the responding practitioner: year of graduation from medical school; administrative district of practice; type of practice (hospital practice exclusively, private practice exclusively or part-
time hospital practice and private practice, here referred to as "mixed practice"). The second part of the questionnaire collected information about the practitioner’s IBD patients and included such items as:

- number of patients with IBD consulting per year and percentage of IBD patients with UC or CD;
- percentage of IBD patients treated with anti-TNF;
- anti-TNF treatments initiated or not by the responding practitioner.

The third part of the questionnaire covered the practitioners’ clinical practices via 12 questions (three to four possible answers per question, with one or more answers accepted per question) (Table 1).

**Statistical analysis**

**Global analysis**

Discrete variables with a normal distribution were expressed as means ± standard deviation or as medians with 25—75% interquartile ranges (IQR). Proportions were expressed as a percentage and 95% confidence interval (95CI). Univariate ANOVA was applied to compare means for variables with a normal distribution, and the Mann—Whitney test in case of abnormal distribution. Fisher’s exact test was applied to derive proportions. Logistic regression multivariate analyses were then applied to variables retained by the univariate analyses. *P* < 0.05 was considered statistically significant. Data were processed using Minitab®, release 14.1 software (Minitab Inc.).

**Subgroup analyses**

Subgroups were compared to look for predictive factors. Four criteria were used to identify eight subgroups:

- year of graduation from medical school before versus after 1978;
- hospital practice versus private or mixed practice;
- number of patients with IBD consulting annually above 10 versus less than 10;
- number of patients with anti-TNF treated annually above 10 versus less than 10.

The items studied were initiation of infliximab, initiation of adalimumab and the 12 aspects of clinical practice. The percentages for each item were first compared by subgroup using univariate ANOVA, and then the variables exhibiting a significant difference were retained for the multivariate logistic regression model.

**Results**

**Response rate**

One hundred questionnaires were mailed-out in January 2008, according to the database of the Conseil national de l’Ordre des médecins (National Council of the Medical Association), 106 gastroenterologists practice in the Lorraine region. This meant that the survey of medical practices should be representative of all gastroenterologists practicing in Lorraine. In April 2008, 36 questionnaires (36%) were returned. A recall letter was then sent to the 64 practitioners who had not returned their questionnaires. In June 2008, 10 more questionnaires were returned. Thus, the overall response rate was 46% (46/100).

**Characteristics of the 46 responding gastroenterologists**

Questionnaires were received from gastroenterologists practicing in the following administrative districts in the Lorraine region: Moselle (*N* = 17, 37%); Meurthe-et-Moselle (*N* = 10, 21.7%); Vosges (*N* = 6, 13%); Haute-Marne (*N* = 3, 6.5%); Haute-Saône (*N* = 3, 6.5%); and Territoire de Belfort (*N* = 1, 2.2%). The administrative district was not stated on six questionnaires (13%). The average year of graduation was 1984 ± 7.9 years. Twenty-one physicians (46.7%, 95CI: 31.5—61.8) practiced exclusively in a hospital setting; 10 (22.2%, 95CI: 9.59—34.9) had private practices and 14 (31.1%, 95CI: 17.0—45.2) had mixed practices. The type of practice was not stated on one questionnaire (2.2%). The percentages of physicians who had initiated, at least once, treatment with infliximab and adalimumab were 76.1% (95CI: 63.3—88.9) and 56.5% (95CI: 41.6—71.4), respectively.

**Characteristics of patients consulting for IBD**

The 46 responding physicians (*N* = 46) reported on a population of 1690 patients consulting for IBD. The median number of patients per physician was 30 (95CI: 20—40). Among this patient population, 42.13% (95CI: 37.15—47.11) had UC and 58.31% (95CI: 53.40—63.22) had CD. The responding physicians (*N* = 46) treated 840 patients with anti-TNF. The median number of these patients per physician was 20 (IQR: 10—30). Among those treated with anti-TNF, the mean percentages with UC and CD were 14.75% (95CI: 9.49—20.01) and 76.97% (95CI: 63.3—88.9), respectively.

**Results of the practitioner survey**

**Global analysis**

This analysis (Table 1) covered the 12 items related to clinical practices, with 36—44 responses obtained for each of the 12 items. For patients with CD who responded to induction therapy with infliximab, 95.5% of the physicians prescribed long-term treatment with injections of infliximab every 8 weeks (item No. 1). If the response to infliximab failed to persist in a patient with luminal CD, 48.6% of the physicians reduced the treatment interval to 6 weeks, 21.6% increased the infliximab dose and 29.7% switched to adalimumab (item No. 2). All practitioners used an induction schedule with adalimumab injections of 80 mg and then 40 mg at weeks 0 and 2; 30% also prescribed regular induction with 160 mg, then 80 mg, at weeks 0 and 3 (item No. 3). In the event of a serious intolerance reaction to infliximab infusion, but without relapse in a patient with luminal CD, 97.2% of the practitioners prescribed an injection every 8 weeks with premedication (hydrocortisone and antihistaminics) before...
Table 1  Responses to the questionnaire (12 items) by the 46 gastroenterologists.
Réponses au questionnaire (12 questions) des 46 gastroentérologues ayant participé à l’enquête de pratique.

<table>
<thead>
<tr>
<th>Practitioner survey questions</th>
<th>Number of practitioners who responded</th>
<th>Number (%) of practitioners per response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Item No. 1:</strong> for a patient with Crohn’s disease responsive to induction therapy with infliximab, what is your approach?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular injections every 6 weeks</td>
<td>44</td>
<td>0</td>
</tr>
<tr>
<td>Regular injections every 8 weeks</td>
<td>42 (92.5)</td>
<td></td>
</tr>
<tr>
<td>Injections if renewed symptoms (treatment as needed)</td>
<td>2 (4.55)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 2:</strong> in the event of relapse after response to infliximab every 8 weeks in a patient with luminal Crohn’s disease, what is your strategy?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase infliximab dose</td>
<td>37</td>
<td>8 (21.6)</td>
</tr>
<tr>
<td>Injections every 6 weeks</td>
<td>18 (48.6)</td>
<td></td>
</tr>
<tr>
<td>Switch to adalimumab</td>
<td>11 (29.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 3:</strong> for Crohn’s disease, what induction regimen(s) of adalimumab do you use?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>160 mg, then 80 mg</td>
<td>40</td>
<td>12 (30)</td>
</tr>
<tr>
<td>80 mg, then 40 mg</td>
<td>40 (100)</td>
<td></td>
</tr>
<tr>
<td>40 mg, then 10 mg</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 4:</strong> in the event of serious intolerance to infliximab without relapse in luminal Crohn’s disease, what is your strategy?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection every 8 weeks with hydrocortisone and antihistaminic premedication before each further injection</td>
<td>36</td>
<td>35 (97.2)</td>
</tr>
<tr>
<td>Injections every 10–12 weeks</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Dose reduction of infliximab</td>
<td>1 (2.78)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 5:</strong> what is your approach for a patient with Crohn’s disease in clinical and biological (normal C-reactive protein) remission after 6 months of the azathioprine–infliximab combination?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continue azathioprine alone</td>
<td>40</td>
<td>11 (27.5)</td>
</tr>
<tr>
<td>Continue azathioprine–infliximab combination</td>
<td>7 (18.5)</td>
<td></td>
</tr>
<tr>
<td>Continue infliximab alone</td>
<td>22 (55.0)</td>
<td></td>
</tr>
<tr>
<td>Stop azathioprine and infliximab and switch to aminosalicylate</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 6:</strong> what exploration(s) do you routinely order before starting anti-TNF treatment?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete pretherapeutic workup</td>
<td>44</td>
<td>11 (25.0)</td>
</tr>
<tr>
<td>Partial pretherapeutic workup</td>
<td>33 (75.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 7:</strong> if the PPD skin test measures 7 mm and the chest X-ray is normal in a patient with no risk factors for tuberculosis, what is your response?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic scan and refer to lung specialist</td>
<td>42</td>
<td>19 (45.20)</td>
</tr>
<tr>
<td>Start anti-TNF without chemoprophylaxis</td>
<td>19 (45.20)</td>
<td></td>
</tr>
<tr>
<td>Chemoprophylaxis before starting anti-TNF</td>
<td>4 (9.52)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 8:</strong> if the PPD skin test measures 11 mm and the chest X-ray is normal in a patient with no risk factors for tuberculosis, what is your response?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic scan and refer to lung specialist</td>
<td>42</td>
<td>32 (76.20)</td>
</tr>
<tr>
<td>Start anti-TNF without chemoprophylaxis</td>
<td>1 (2.38)</td>
<td></td>
</tr>
<tr>
<td>Chemoprophylaxis before starting anti-TNF</td>
<td>9 (21.40)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 9:</strong> What is your approach for a patient with Crohn’s disease in clinical and biological (normal C-reactive protein) remission after 1 year of anti-TNF?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stop anti-TNF</td>
<td>42</td>
<td>15 (35.7)</td>
</tr>
<tr>
<td>Continue anti-TNF</td>
<td>27 (64.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 10:</strong> in 2008, for a patient unresponsive to standard medical treatment (corticosteroids, immunosuppressors), which anti-TNF would you give as first-line treatment?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>44</td>
<td>12 (27.3)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>32 (72.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Item No. 11:</strong> what is your approach to a patient with acute pharyngitis and a temperature of 37 °C?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-TNF injections with antibiotic cover</td>
<td>43</td>
<td>11 (25.6)</td>
</tr>
</tbody>
</table>
each infusion (item No. 4). For patients with quiescent CD after 6 months of the azathioprine—infliximab combination, 55.0% of the physicians interrupted the azathioprine, but maintained infliximab alone, 27.5% used azathioprine alone and 17.5% continued the two-drug combination (azathioprine plus infliximab) (item No. 5).

Only one fourth of the responding physicians ordered a complete pretherapeutic workup (Table 2) (item No. 6). If the purified protein derivative (PPD) skin test measured 7 mm in a patient with a normal chest X-ray and no risk factors for tuberculosis, 45.2% of the physicians routinely ordered a thoracic scan and referred the patient to a lung specialist; the same proportion (45.2%) initiated anti-TNF treatment without chemoprophylaxis (item No. 7). If the PPD skin test measured 11 mm, then 76.2% of the physicians ordered a thoracic scan and referred the patient to a lung specialist, and 21.4% started chemoprophylaxis before initiating the anti-TNF treatment, while only 2.4% started anti-TNF treatment without chemoprophylaxis (item No. 8). For patients with quiescent CD after 1 year of an anti-TNF regimen, 64.3% of the physicians continued the anti-TNF treatment and 35.7% stopped it (item No. 9). For CD patients unresponsive to standard medical treatment (steroids, immunosuppressors) requiring anti-TNF treatment, 72.7% of the physicians introduced infliximab as the first-line treatment, while 27.3% opted for adalimumab (item No. 10). For patients with quiescent CD after 1 year of an anti-TNF regimen, 64.3% of the physicians continued the anti-TNF treatment and 35.7% stopped it (item No. 9). For CD patients unresponsive to standard medical treatment (steroids, immunosuppressors) requiring anti-TNF treatment, 72.7% of the physicians introduced infliximab as the first-line treatment, while 27.3% opted for adalimumab (item No. 10). In the event of acute pharyngitis without fever (37°C), 58.1% of the physicians initiated antibiotic therapy and delayed the anti-TNF injection, while 25.6% prescribed anti-TNF with antibiotic coverage (item No. 11). In the event of urinary tract infection without fever (37°C), 44.2% of physicians started an antibiotic regimen with the anti-TNF injection and 46.5% did not prescribe antibiotic coverage (item No. 12).

### Subgroup analysis

**Year of graduation.** Practitioner responses to each item were analyzed comparing the subgroups of those who graduated from medical school before 1978 and after 1978. Univariate analysis showed that the only difference between these two subgroups involved initiation of infliximab treatment: all 10 physicians who had graduated before 1978 initiated infliximab treatment at least once versus 65.6% (21/32) of those in the second subgroup ($P = 0.041$) (Table 3). This difference was no longer significant in the multivariate logistic regression model.

**Hospital and/or private practice.** On univariate analysis, there was a statistically significant difference between the subgroups of practitioners according to four variables:

- infliximab had been initiated by 95.2% (20/21) of the practitioners with exclusively hospital practices versus 58.3% (14/24) of those with private or mixed practices ($P = 0.005$);
- similarly, adalimumab treatment had been initiated by 71.4% (15/21) of the hospital practitioners versus 41.3% (10/24) of those with private or mixed practices ($P = 0.035$);
- for first-line prescription of anti-TNF for refractory CD (item No. 10), the proportion of hospital practitioners was 94.7% (18/19) versus 54.2% (13/24) of the others ($P = 0.005$);
- on multivariate analysis, logistic regression retained only the difference concerning first-line introduction of infliximab and adalimumab (item No. 10).

**Number of patients/year consulting for IBD.** On univariate analysis, there was no statistically significant difference as regards the 12 items between gastroenterologists who had more versus less than 20 patients consulting for IBD per year.

**Number of patients/year given anti-TNF.** On univariate analysis, two items—infliximab initiation, and ordering a complete pretherapeutic workup (item No. 6)—were influenced by the number of patients given anti-TNF per year. Infliximab was initiated at least once by 83.3% (25/30) of physicians who treated more than 10 patients/year with anti-TNF versus only 37.5% (3/8) for those treating less than 10 patients/year with anti-TNF ($P = 0.009$). A complete pretherapeutic assessment (item No. 6; Table 2) was ordered by 13.4% (4/30) of physicians who treated more than 10 patients/year versus 57.1% (4/7) of those who treated less patients/year with anti-TNF.
Table 3
Results of practitioner subgroup analyses.

<table>
<thead>
<tr>
<th>Survey item</th>
<th>Graduation before 1978</th>
<th>Exclusive hospital practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever prescribed first-line infliximab?</td>
<td>0.041</td>
<td>NS</td>
</tr>
<tr>
<td>First-line infliximab (item No. 10)</td>
<td>0.025</td>
<td>NS</td>
</tr>
<tr>
<td>Pretherapeutic assessment (item No. 6)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant (P < 0.05 considered significant).

than 10 patients/year with anti-TNF (P = 0.027). These statistically significant differences on univariate analysis were not significant on multivariate analyses.

Discussion

This is the first study evaluating the clinical practices of nonacademic gastroenterologists prescribing anti-TNF for IBD. The 46 gastroenterologists who responded to this survey had treated 1690 patients (median: 30 patients per physician). It should be noted, however, that patients might have consulted more than one gastroenterologist, especially hospital practitioners. All of the responding gastroenterologists had experience with the use of anti-TNF for IBD and, among those who graduated from medical school before 1978, a larger proportion had initiated infliximab at least once. This finding may, however, reflect a study bias rather than the clinical practices of all gastroenterologists.

In patients responding to infliximab induction therapy, more than nine out of 10 physicians prescribed injections every 8 weeks. Every 8 weeks, a practice that is in agreement with the current expert recommendations. In 2008, it is considered preferable to prescribe a routine infusion of infliximab every 8 weeks rather than an episodic treatment, which is more immunogenic and less effective in terms of clinical response and endoscopic healing [6—8].

In the case of a CD patient who initially responds to infliximab, then relapses, around half of the responding physicians preferred to shorten the injection interval to 6 weeks; the remainder opted for higher-dose infliximab (21.6%) or switch to adalimumab (29.7%). It is worth noting that there is no scientific evidence that a shorter interval between infusions is an effective strategy; only increasing the infliximab dose from 5 to 10 mg/kg has proven effective in refractory luminal fistular CD, as shown mainly by analyses of subgroups of patients using data from controlled randomized trials versus placebo [5,9]. One small-scale study also found that an increased infliximab dose was effective in such patients [10]. Around 30% of practitioners switched to adalimumab when their patients with luminal CD relapsed on infliximab, an approach that is not consistent with the current expert recommendations. As these are the only two anti-TNF agents available for CD at this time (2008), most experts favor the first-line use of an increased dose and/or reduced infusion interval rather than switching to the other anti-TNF [11], despite the lack of evidence to support this approach. Indeed, the only data available—from a model indirectly comparing infliximab and adalimumab—are difficult to interpret [12].

For the acute treatment of CD, all of the responding practitioners used an induction schedule with subcutaneous injections of 80 mg, then 40 mg on weeks 0 and 2, and 30% also prescribed 160 mg, then 80 mg, doses. Only the 160 mg, then 80 mg, regimen on weeks 0 and 2 has demonstrated significantly greater efficacy than placebo as an induction treatment [13]. Nevertheless, and despite these results, the European Drug Agency has given its marketing approval for adalimumab with the 80/40 mg schedule for CD, while authorizing prescribers to opt for the 160/80 mg schedule if a more rapid response is needed. In the US, the Food and Drug Administration (FDA) has given its approval for
adalimumab solely with the 160/80 mg schedule, basing its arguments on the CLASSIC-I trial [13]. The practices of the 46 physicians who responded to our survey may therefore be explained by regulatory decisions.

In the event of a serious intolerance reaction to infliximab, all of the physicians used a premedication regimen of hydrocortisone and antihistamines before each infusion. Again, although the efficacy of this practice has not been formally demonstrated and given a response of, at most, a reduction in the development of anti-infliximab antibodies in CD and rheumatology patients, it is, nevertheless, advocated by most practitioners. It should be noted that experts currently recommend switching to adalimumab in the event of a serious reaction to infliximab as the former has proved to be effective and well tolerated [14]. Our questionnaire did not include an item for this option.

For CD patients with quiescent disease after 6 months of an azathioprine–infliximab combination, about half of the practitioners withdrew azathioprine and continued the infliximab on its own, a strategy that has recently proved to result in a clinical response that is similar, at 2 years, to giving the two agents in combination. Serum infliximab levels were, however, lower in the group not given azathioprine—with consequences that, in the long run in terms of relapse, remain unknown [15]. This suggests that the 46 physicians who responded to this question were well aware of the most recent data concerning this subject. A bridge strategy (interrupting infliximab and continuing azathioprine) was preferred by about one quarter of the physicians. This strategy has proven efficacy at 1 year [16], but has been found to be ineffective in the longer term [17] and, so, cannot be recommended. Finally, 17.5% of the practitioners persisted with the azathioprine–infliximab combination. However, once again, in the light of 17 cases of hepatosplenic T cell lymphoma, with devastating prognoses, seen mainly in young patients given thiopeurines and infliximab [18], the long-term use of this combination cannot be recommended—especially as, according to post hoc analyses of large-scale trials [5,9], the efficacy of infliximab would not be affected by concomitant immunomodulating treatment. The eagerly awaited results of the international Study of Immunomodulator-Naïve Patients in Crohn’s Disease (SONIC) trial are expected to be available soon and should provide a clear answer to this question.

A complete pretherapeutic assessment, recommended by experts and pharmaceutical companies [11], was ordered by only one fourth of our responding practitioners. Paradoxically, it was those who treated more than 10 patients/year with anti-TNF who ordered the fewest workups. This finding underscores the importance of the need for better information regarding the risks of opportunistic infections, tuberculosis and reactivation of viral hepatitis by physicians prescribing TNF antagonists.

In the event of a PPD skin test measuring 7 mm (or more than 5 mm), nearly half of the practitioners initiated anti-TNF treatment without antituberculosis prophylaxis. However, this proportion fell to 2.4% if the skin test measured 11 mm. In February 2002, the French Health Product Safety Agency (Agence française de sécurité sanitaire des produits de santé [Afssaps]) issued its nationwide recommendations for the prevention and management of tuberculosis in patients given infliximab, followed by an update in July 2005. The main change was to start chemoprophylaxis when the skin test measured more than 5 mm instead of more than 10 mm [11]. This change was the result of the observation reported by the recherche anti-TNF et infections opportunistes (RATIO) that certain cases of tuberculosis have arisen in patients taking anti-TNF with a skin test measuring 5–10 mm. Our findings show that these recommendations were not being followed by around half of our responding practitioners.

For an asymptomatic patient who has been taking anti-TNF for 1 year, nearly two thirds of practitioners continued the treatment, an approach that is in agreement with most expert recommendations. Indeed, a growing body of evidence shows that the clinical benefit of infliximab continues beyond 1 year [19]. Nevertheless, 1 year is the longest follow-up reported in placebo-controlled trials, so it remains an option to stop anti-TNF after a year. The results of the Groupe d’étude thérapeutique des affections inflammatoires du tube digestif (GÉTAIM) trial STORI will soon be available and are likely to provide greater insight in this issue.

When refractory disease warrants anti-TNF treatment, nearly three quarters of our responding practitioners introduced infliximab as the first-line treatment, and more than nine out of 10 hospital practitioners introduced first-line infliximab versus half (54.2%) of those in private or mixed practices. This difference remained significant on multivariate analyses. However, there is no data on comparative efficacy for these two compounds as first-line treatment for refractory luminal CD, so both therapeutic options remain acceptable. Adalimumab has been available since 2008 for home care (administered by the patient or a nurse). Thus, some patients might prefer having their subcutaneous injections at home, while consulting their hospital or private physician regularly. Hospital physicians might decide to use infliximab first to better guarantee patient follow-up during short, day hospitalizations for the infusion every 8 weeks. This survey did not provide any detailed information on this issue.

Finally, when faced with an afibrile patient presenting with acute pharyngitis or urinary tract infection, the practitioners had various responses. They appeared to be more prudent in cases of pharyngitis, as 58.1% initiated antibiotics and delayed the anti-TNF injections, and 44.2% did the same for urinary tract infection. These results underscore the need for precise guidelines concerning the management of infections in patients taking anti-TNF. The consensus of the European Crohn’s and Colitis Organization (ECCO) workshop, held in December 2007, on the management of infection in patients with IBD undergoing immunosuppressor or immunomodulator treatments should be published in extenso shortly, thereby allowing practitioners to adopt a more evidence-based approach to these patients.

In conclusion, the results of our survey—albeit including a limited number of responses (N = 46)—indicate that, although nonacademic gastroenterologists in hospitals and/or private practices in the Lorraine region generally comply with certain recommendations concerning, in particular, the use of immunosuppressive agents in combination with anti-TNF and the prescription of anti-TNF per se, they would benefit from further education and information on
other treatment considerations, such as the management of concomitant infections and the ordering of a complete pretherapeutic patient assessment.

Conflict of interest

L. P.-B. has received consulting fees from Abbott Laboratories and UCB Pharma, lecture fees for speaking at continuing medical education events from Centocor, and grant support from UCB Pharma.

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